3D quantification of brain microvessels exposed to heavy particle radiation

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DOI: https://doi.org/10.1088/1742-6596/186/1/012087

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2009 J. Phys.: Conf. Ser. 186 012087

(http://iopscience.iop.org/1742-6596/186/1/012087)

Journal of Physics: Conference Series **186** (2009) 012087 doi:10.1088/1742-6596/186/1/012087

3D quantification of brain microvessels exposed to heavy particle radiation

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Abstract. Space radiation with high energy particles and cosmic rays presents a significant hazard to spaceflight crews. Recent reviews of the health risk to astronauts from ionizing radiation concluded to establish a level of risk which may indicate the possible performance decrements and decreased latency of late dysfunction syndromes (LDS) of the brain. A hierarchical imaging approach developed at ETH Zürich and PSI, which relies on synchrotron based X-ray Tomographic Microscopy (SRXTM), was used to visualize and analyze 3D vascular structures down to the capillary level in their precise anatomical context. Various morphological parameters, such as overall vessel volume, vessel thickness and spacing, are extracted to characterize the vascular structure within a region of interest. For a first quantification of the effect of high energy particles on the vasculature we scanned a set of 6 animals, all of same age. The animals were irradiated with 1 Gy, 2 Gy and 4 Gy of 600MeV ^{56}Fe heavy particles simulating the space radiation environment. We found that with increasing dose the diameter of vessels and the overall vessel volume are decreased whereas the vessel spacing is increased. As these parameters reflect blood flow in three-dimensional space they can be used as indicators for the degree of vascular efficiency which can have an impact on the function and development of lung tissue or tumors.

1. Introduction

Space radiation with high energy particles and cosmic rays presents significant health hazards to spaceflight crews. There is a need to establish a level of risk associated with exposure to space radiation and the potential development of late dysfunction syndromes (LDS) such as Alzheimers Disease (AD) and stroke. This risk assessment is similar to increases found for carcinogenesis after radiation exposure. To evaluate the structural changes in the CNS micro-vasculature after radiation exposures similar to those expected in long term space flight we use an established genetic model of Alzheimer disease.

2. Methods

The temporal progression of the vascular changes was studied using a transgenic (tg) Alzheimer disease mouse model overexpressing the amyloid percussor protein (APP). Vascular corrosion casts (VCC) (fig. 1.b), produced three weeks after $0, 1, 2, 4\,\mathrm{Gy}$ ^{56}Fe radiation exposure (fig. 1.a), were imaged (fig. 1.c, 1.e) with synchrotron radiation based X-ray tomographic

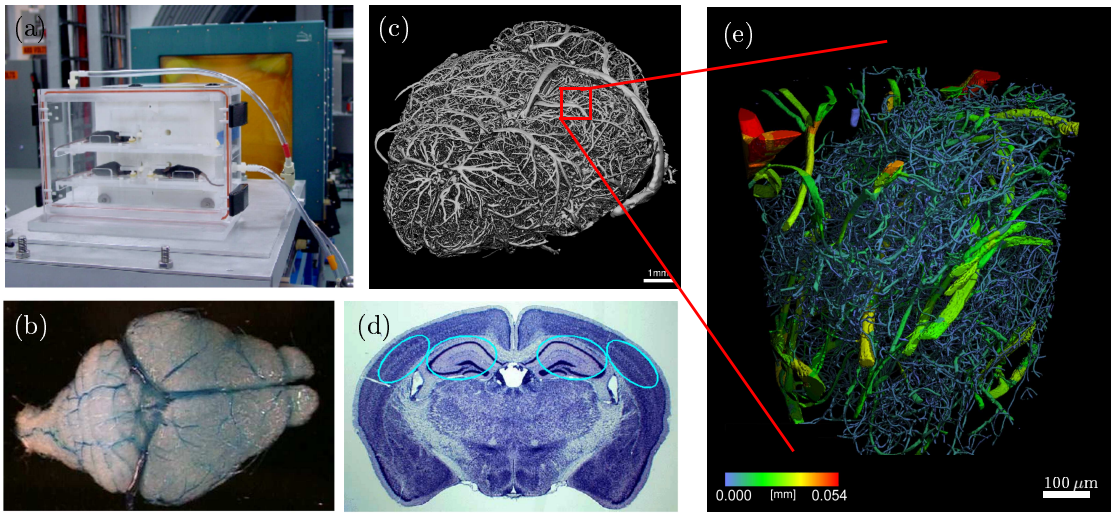

Figure 1. (a) Irradiation of animals at Nasa Space Radiation Laboratory at Brookhaven National Laboratory; (b) Vascular corrosion cast produced 3 weeks after irradiation; (c) 3D rendering of the brain vasculature scanned with a pixel size of 12 μm at the TOMCAT beamline of the Swiss Light Source (SLS) at Paul Scherrer Institute; (d) Regions targeted for morphometric evaluation of the vasculature; (e) 3D rendering of region from left posterior hippocampus with a pixelsize of 0.78 μm scanned at the TOMCAT beamline. Vessel thickness has been color coded.

microscopy (SRXTM). Hippocampal and cortical morphological parameters including vessel thickness, volume, spacing, length and number of vessels per volume were calculated in APP mice.

3. Results

A previous study [1] has shown significant alterations in the micro-vasculature structures of APP tg mice. In our work, quantification of heavy particle (^{56}Fe) irradiation on the micro-vasculature revealed that as dose increased the vessel diameter and the overall vessel volume decreased (Fig. 2, 3), thus increasing the inter-vessel spacing. Quantitative analysis indicated that with increasing irradiation dose more vessels with diameters of $7-30\,\mu$m are lost. In contrast, the number and volume of capillaries was increased in animals irradiated with 2 Gy.

4. Discussion and Outlook

The dose dependent decrement in vessel density indicates an incremental vascular insufficiency. Part of the vascular loss appears to be compensated by processes like angiogenesis and/or vascular re-modeling (Fig. 2, 3). Thus, alterations in the vasculature after exposure to radiation can be important factors of neuro-degenerative diseases. How the radiation induced changes evolve over time is part of the ongoing research.

Acknowledgement

Supported by a NASA NSCOR # NNJ04HC9OG

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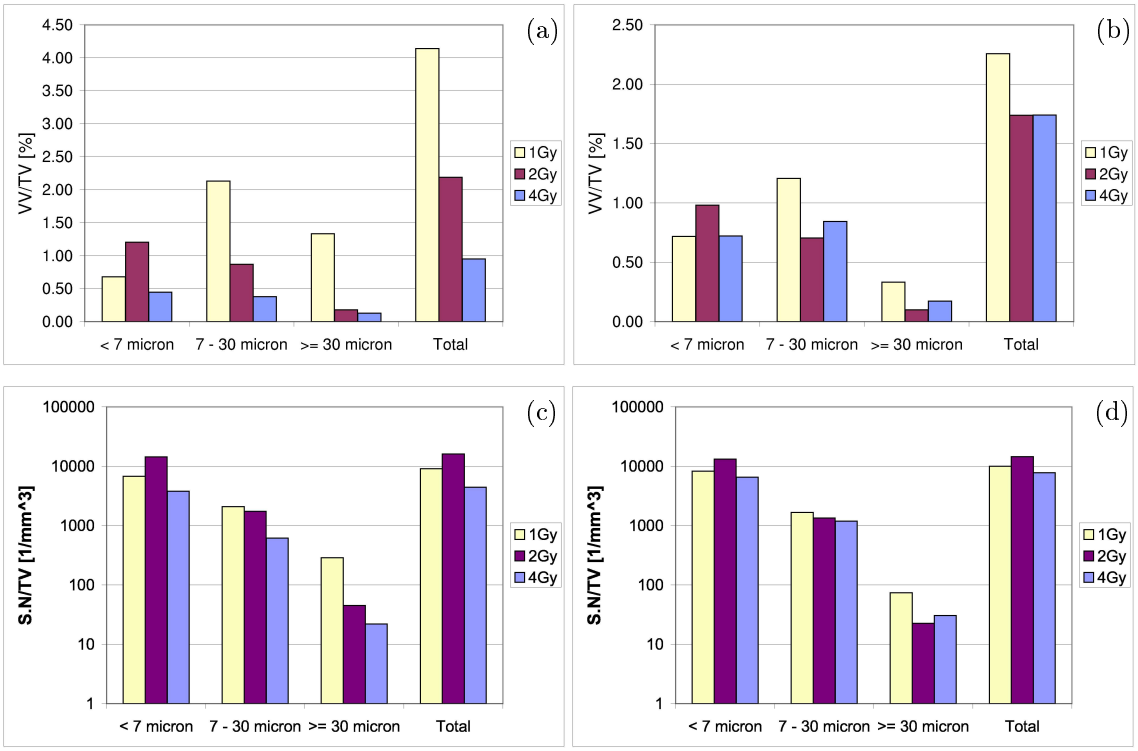

Figure 2. The plots (a) and (b) depict the ratios between the vessel volume (VV) and the tissue volume (TV) for a region of interest (ROI) located in the right anterior hippocampus (RAHPC) (a) and the average of all analyzed ROI (b). The corresponding numbers of vessels (S.N) per TV are plotted in (c) for RAHPC and (d) for all ROI. For the animals irradiated with 2 Gy ^{56}Fe the volume and number of capillaries (Diameter $\leq 7\,\mu$m) is increased. It appears that part of the loss of vessels is compensated by processes like angiogenesis and vascular remodeling.

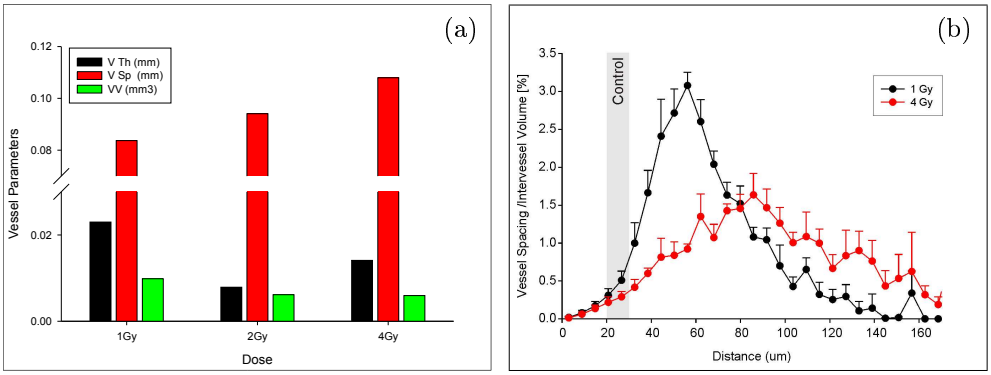

Figure 3. Dose dependent changes in brain vasculature: (a) Vessel spacing (V Sp) increases with dose while vessel volume (VV) and thickness (V Th) decrease; (b) The histograms of the distribution of the vessel spacing reveal a shift to increasing vessel distances per volume with increased doses;